

REMARKS**Summary of the Amendments**

By the foregoing amendment, claims 1, 2 and 4 are amended, and claims 3, 5 and 6 are canceled, whereby claims 1, 2, 4, and 7-9 remain pending. Of the pending claims, claim 1 is independent. Applicant notes that any canceled subject matter has been canceled without prejudice or disclaimer, and Applicant reserves the right to re-introduce the subject matter in this or other applications.

Support for the amendments to the claims can be found, for example, in the originally filed specification and claims, and is also inherent therein. Support for the amendment to claim 1 can be found, for example, in originally filed claim 6. Support for the amendment to claim 2 can be found, for example, in originally filed claim 3. Support for the amendment to claim 4 can be found, for example, in originally filed claim 2. Applicant submits that no new matter is added.

Further, any amendments to the claims which have been made in this response and which have not been specifically noted to overcome a rejection based upon the prior art, should be considered to have been made for a purpose unrelated to patentability, and no estoppel should be deemed to attach thereto.

Information Disclosure Statement

Applicant thanks the Examiner for consideration of the disclosure statements filed August 2, 2005 and August 10, 2006, by returning initialed copies of the Forms PTO-1449 submitted therein.

Claim of Priority

Applicant thanks the Examiner for the acknowledgement of Applicants' claim of priority. However, Applicant notes that the present application is a National Stage PCT application so that the acknowledgement of the claim of priority should indicate that the certified copies of the priority documents were received from the International Bureau (*i.e.*, box 12(a)(3) of the Office Action Summary should be checked). Therefore, Applicant respectfully requests that the Examiner check box 12(a)(3) in the next communication from the Office.

RESPONSE TO CLAIM REJECTIONS**1. Response to Rejection under 35 U.S.C. § 112, second paragraph**

The Office Action rejects claim 5 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. In particular, the Office Action submits that the phrase "wherein the vegetable oil is a vegetable oil having an iodine value higher than 100 or a mixture thereof" is confusing.

In response, and without expressing any agreement or acquiescence with the rejections of record, Applicant has canceled claim 5 to advance prosecution of the application. Therefore, Applicant respectfully requests withdrawal of the 35 U.S.C. § 112, second paragraph rejection of claim 5.

2. Response to Rejection under 35 U.S.C. § 103(a)

The Office Action rejects claims 1-9 under 35 U.S.C. § 103(a) as being unpatentable over Muto et al. (New England Journal of Medicine, hereafter “MUTO-1”), and further in view of Muto et al. (U.S. Pat. No. 5,852,057, hereafter “MUTO-2”), Rinaldi et al. (U.S. Pat. No. 5,891,470, hereafter “RINALDI”), and Hitoshi et al. (JP 63-166824, hereafter “HITOSHI”).

The Office Action submits that MUTO-1 discloses the claimed 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid and opaque capsules made of soft gelatin (p. 1562 and Figure 1), but does not explicitly teach that the capsule preparation comprises the particular vegetable oils, surfactants, and light blocking agents as claimed. The Office Action submits that MUTO-2 discloses the claimed 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid which is an acyclic retinoid (col. 2, lines 29-35), and a placebo capsule of peanut oil (col. 3, lines 1-10), but does not explicitly disclose the active capsule preparation in combination with peanut or another vegetable oil. The Office Action further submits that RINALDI discloses that retinoids are sensitive to light

and should be stored in opaque or colored containers (col. 1, lines 9-18). Lastly, the Office Action submits that HITOSHI discloses a semi transparent soft gelatin capsule comprising titanium dioxide which is useful for encapsulating light unstable drugs (English Abstract).

In view of the teachings of the cited documents, the Office Action submits that it would have been obvious to prepare a soft, opaque gelatin capsule comprising 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid and a vegetable oil based upon the beneficial teachings of MUTO-1 that such a capsule is “useful in treating hepatocellular carcinoma.” (Office Action, p. 4).

Applicant respectfully requests withdrawal of the obviousness rejection in view of the following remarks. Applicant respectfully submits that a *prima facie* case of obviousness is not established by MUTO-1, and further in view of MUTO-2, RINALDI, and HITOSHI for at least the following reasons. A *prima facie* case of obviousness requires:

- a) the presence of all claimed elements,
- b) the motivation to combine the separate reference teachings, and
- c) a reasonable expectation of success.

The Office Action fails to establish any of these requirements.

First, regarding the presence of all claimed elements, Applicant respectfully submits that the requirement that all claimed elements be taught or suggested in the cited documents has not been met.

For instance, none of the cited documents disclose or suggest at least “vegetable oil comprising soybean oil, sesame oil, or a mixture thereof,” as recited in dependent claim 6, and presently recited in independent claim 1. Therefore, the requirement that all claimed elements be taught or suggested in the cited documents has not been met, and a *prima facie* case of obviousness has not been established. Accordingly, for at least this reason, the 35 U.S.C. § 103 rejection of claims 1-9 over MUTO-1, and further in view of MUTO-2, RINALDI, and HITOSHI should be withdrawn.

Applicant further submits that the Office Action fails to provide sufficient motivation as to why the documents should be combined to arrive at the presently claimed invention.

For example, both the primary document of MUTO-1, which discloses the compound 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid, and the secondary document of MUTO-2, which is discussed in the specification of the present application, fail to disclose the stability problem of the claimed compound.¹ In addition, the tertiary

¹ Applicant notes that the Office Action correctly submits that MUTO-2 discloses a capsule containing the compound 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid is administered to patients, and a placebo capsule containing peanut oil alone is administered to patients, but MUTO-2 does not disclose the active capsule preparation (with 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid) contained peanut oil or

and quaternary documents of RINALDI and HITOSHI also fail to disclose or suggest solving the stability problem of the compound 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid.

Thus, Applicant respectfully submits that the motivation set forth in the Office Action, *i.e.*, “based on the beneficial teachings of [MUTO-1] that such capsule is useful in treating hepatocellular carcinoma” (Office Action, p. 4), is insufficient motivation to establish a *prima facie* case of obviousness, because none of the cited documents disclose using at least the claimed soybean oil, sesame oil, or a mixture thereof to solve the stability problems associated with (2E,4E,6E,10E)-3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid.

Moreover, Applicant respectfully submits that in order to support the conclusion that the claimed invention is either anticipated or rendered obvious over the cited documents, the cited documents must either expressly or inherently teach the claimed invention or the Examiner must present a convincing line of reasoning why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references. Ex parte Clapp, 227 U.S.P.Q. 972 (B.O.A. 1985).

In addition, while a *prima facie* case of obviousness has not been established, whereby the rejection should be withdrawn for at least this reason, Applicant respectfully

another vegetable oil. (*See*, Office Action, p. 3). Applicant respectfully submits that the Office Action incorrectly assumes that the capsule comprises peanut oil in addition to the active ingredient (*i.e.*, the compound 3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid).

directs the Examiner to the results shown in Tables 2 and 3 of Applicant's specification relating to the superior advantageous effects of soybean oil and sesame oil over peanut oil and MCT for storage of NIK-333 ((2E,4E,6E,10E)-3,7,11,15-tetramethyl-2,4,6,10,14-hexadecapentaenoic acid) at 25°C and 40°C, respectively. (*See, e.g.*, Applicant's specification at Tables 2 and 3).

Moreover, Applicant provides the following additional data below in Comparison Tables 1 and 2 which, when compared to Tables 2 and 3 in the present specification (and the claimed invention), demonstrate that the below noted oils (*i.e.*, olive oil, rape oil, and safflower oil) failed to provide high stability of NIK-333 for example at 25°C and 40°C, as compared to Applicant's recited subject matter including soybean oil, sesame oil or mixtures thereof which exhibits advantageous stability. (*Compare, e.g.*, Tables 2 and 3 of the present specification and Comparison Tables 1 and 2 below).

Comparison Table 1: Experimental Stability Results

	25°C storage (NIK-333 residual rate (%))		
	Storage period(week)		
	0	2	4
olive oil	100.0±0.00	98.7±1.00	95.0±1.53
rape oil	100.0±0.00	97.6±1.72	93.8±1.70
safflower oil	100.0±0.00	98.5±1.42	94.1±1.40

Comparison Table 2: Experimental Stability Results

40°C storage (NIK-333 residual rate (%))			
	Storage period (week)		
	0	2	4
olive oil	100.0±0.00	97.0±1.85	91.3±5.18
rape oil	100.0±0.00	97.8±1.46	89.5±2.47
safflower oil	100.0±0.00	89.9±1.36	77.2±0.60

Accordingly, for at least the foregoing reasons, the 35 U.S.C. § 103 rejection of claims 1-9 over MUTO-1, and further in view of MUTO-2, RINALDI, and HITOSHI should be withdrawn.

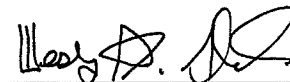
CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow each of the pending claims. Applicant therefore respectfully requests that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully Submitted,
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